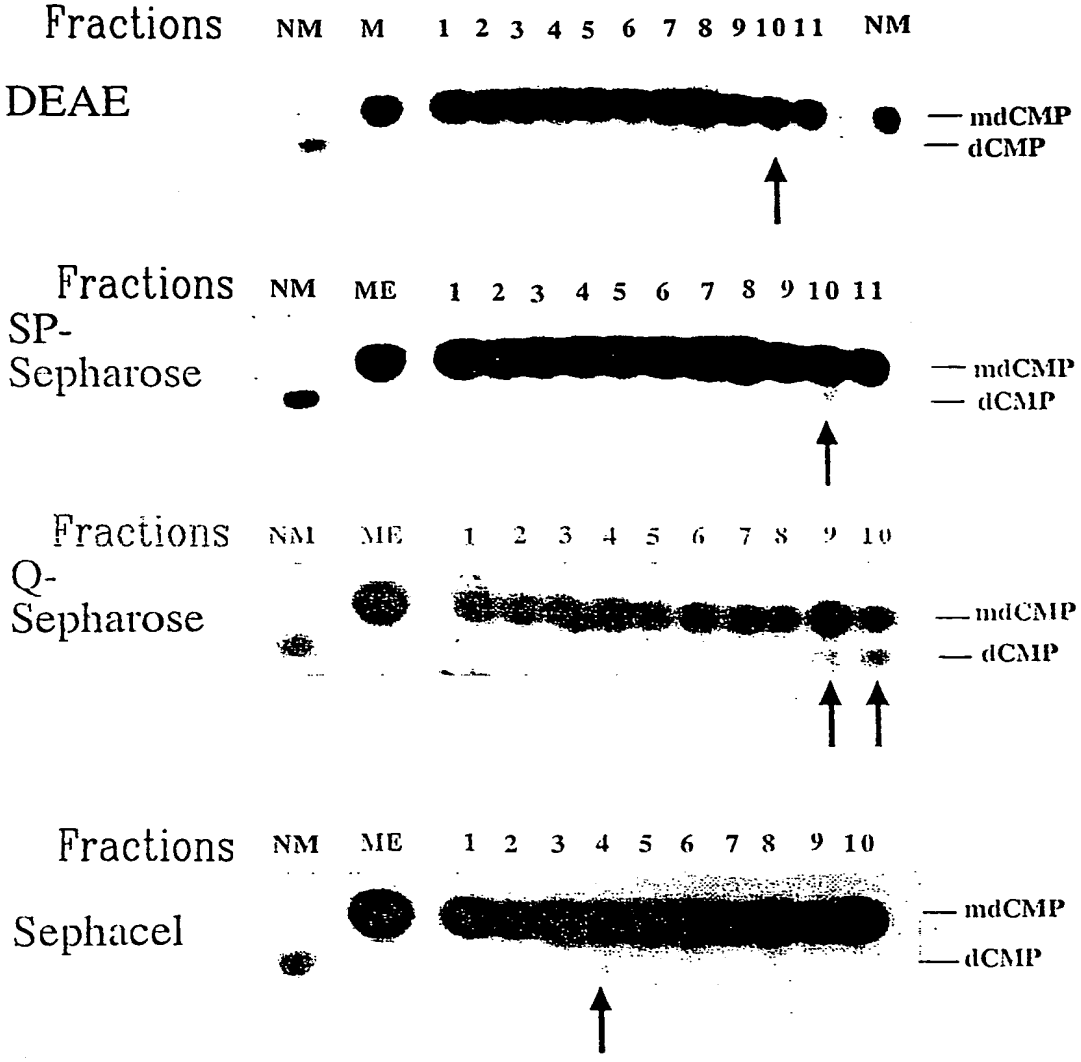
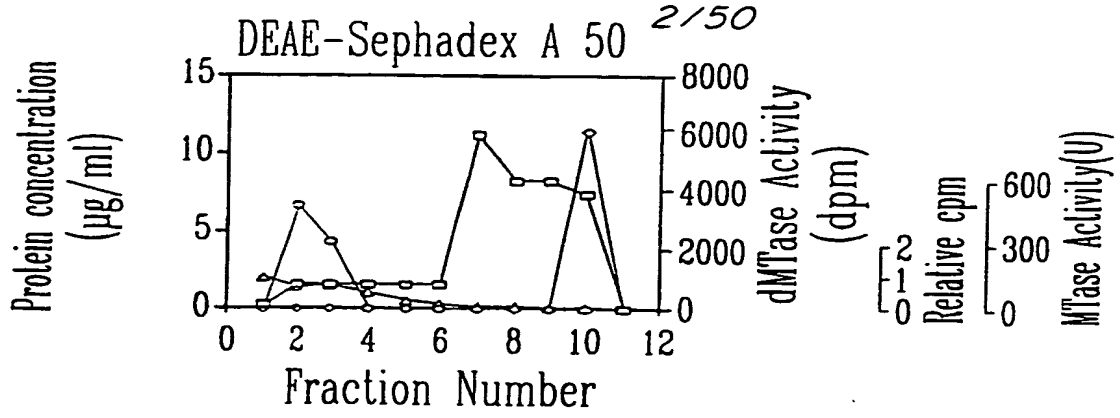
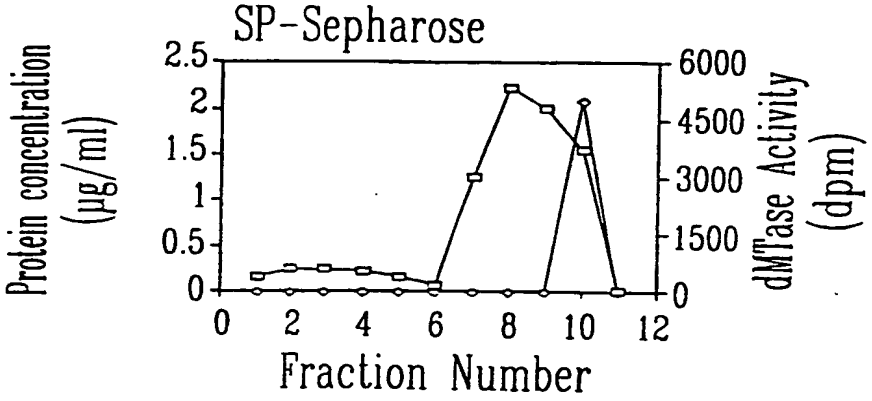
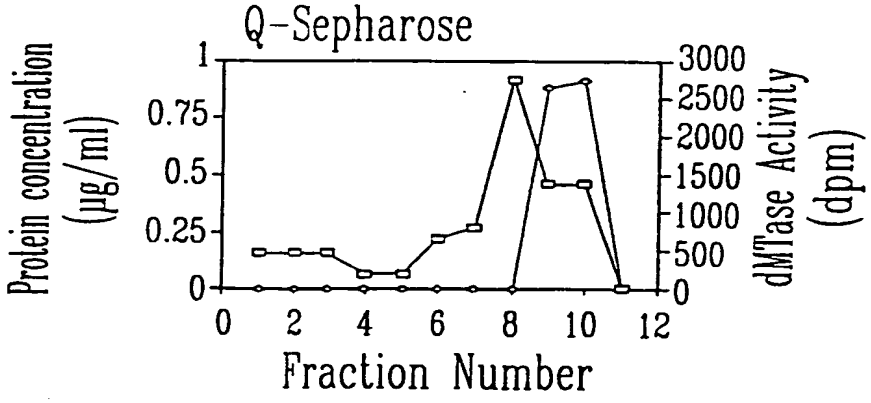


Fig. 1A







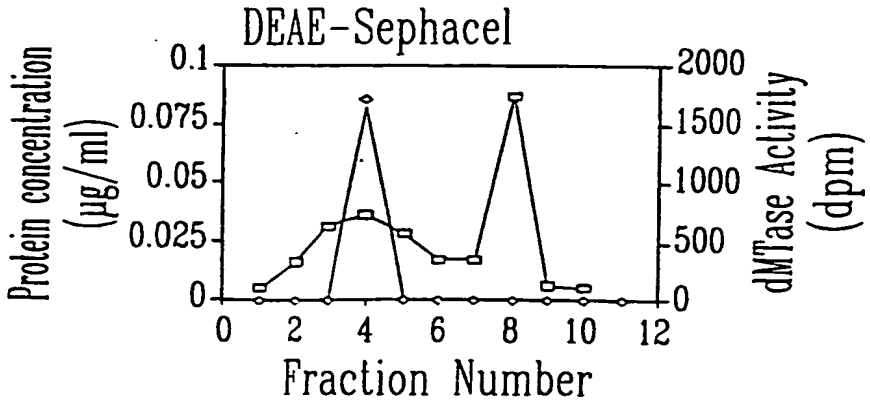


Fig 1B

FIG. 2A
FIG. 2B
— dCMP
— mdCMP
NM
ME
30 min
45 min
1 h
2 h
3 h
24 h
DEAE-Sephadex
S-Sepharose
Q-Sepharose
Sephacel
ddCTP
mdCTP
-RNase
Proteinase K

picomole cytosine formed
1.5
1.0
0.5
0
0
50
100
150
200
Time (min.)
Volatile Assay
CpG Assay
Methyl residues removed (dpm)
4000
3000
2000
1000
0

Fig. 2D

Methyl residues removed (dpm)
5000
4000
2000
1000
0
dMTase - + + -
ProteinaseK - + - +
RNase + + - +

Fig. 2E

Fig - 3A

mdCMP
dCMP
NM
ME
+ dMTase
+dMTase + M. Sss1

Fig - 3B

meC
C
NM
ME
+ dMTase
+dMTase + M. Sss1
1st
2nd

dCTP
- V PDS
N.E.
0
60
120
dCMP
dCDP
dCTP
origin
+ V PDS
+RNase
-RNase
NM
MH
mdCMP
dCMP
dGTP
- V PDS
N.E.
0
60
120
+RNase
dGMP
dGTP
origin
Labeled nucleotide:
[α32P]-dCTP
Labeled nucleotide:
[α32P]-dGTP
*pmCpGp*mCpG
pmC*pGpmC*pG

FIG. 5E

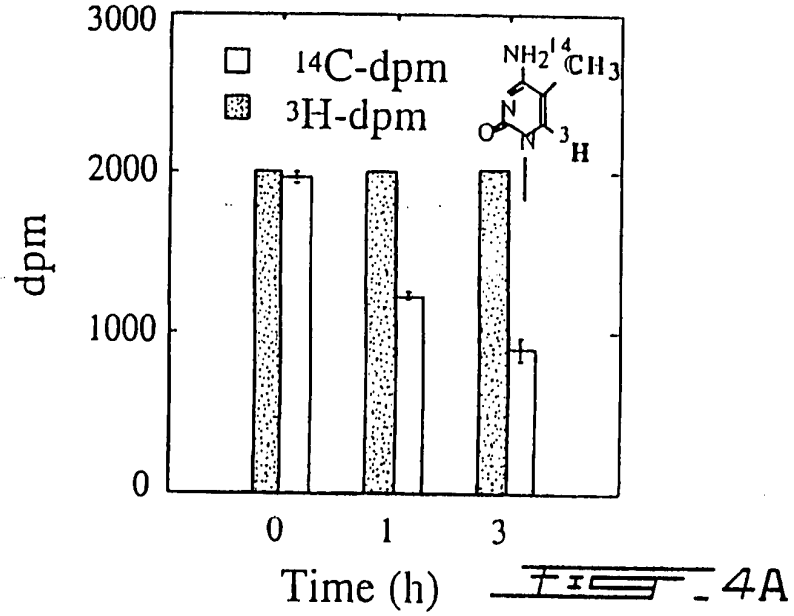
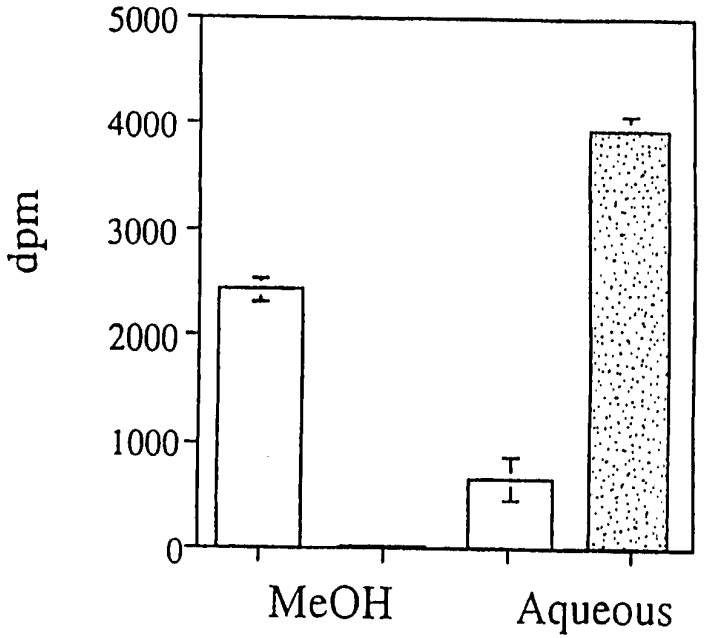


Fig 4A



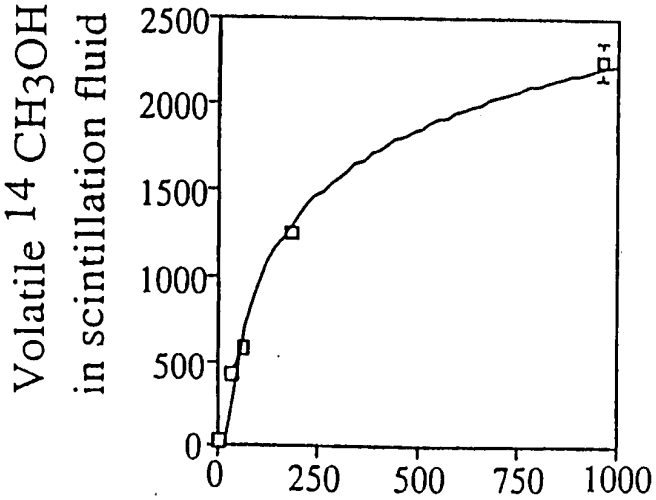


Fig 4C

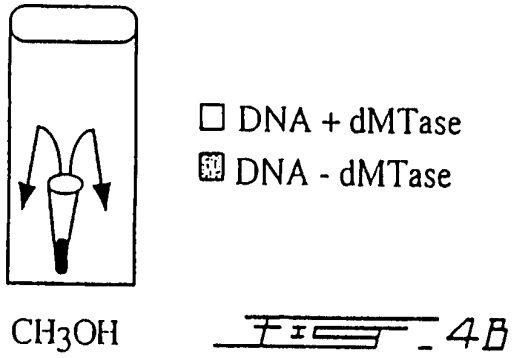


Fig 4B

Fig. 4D

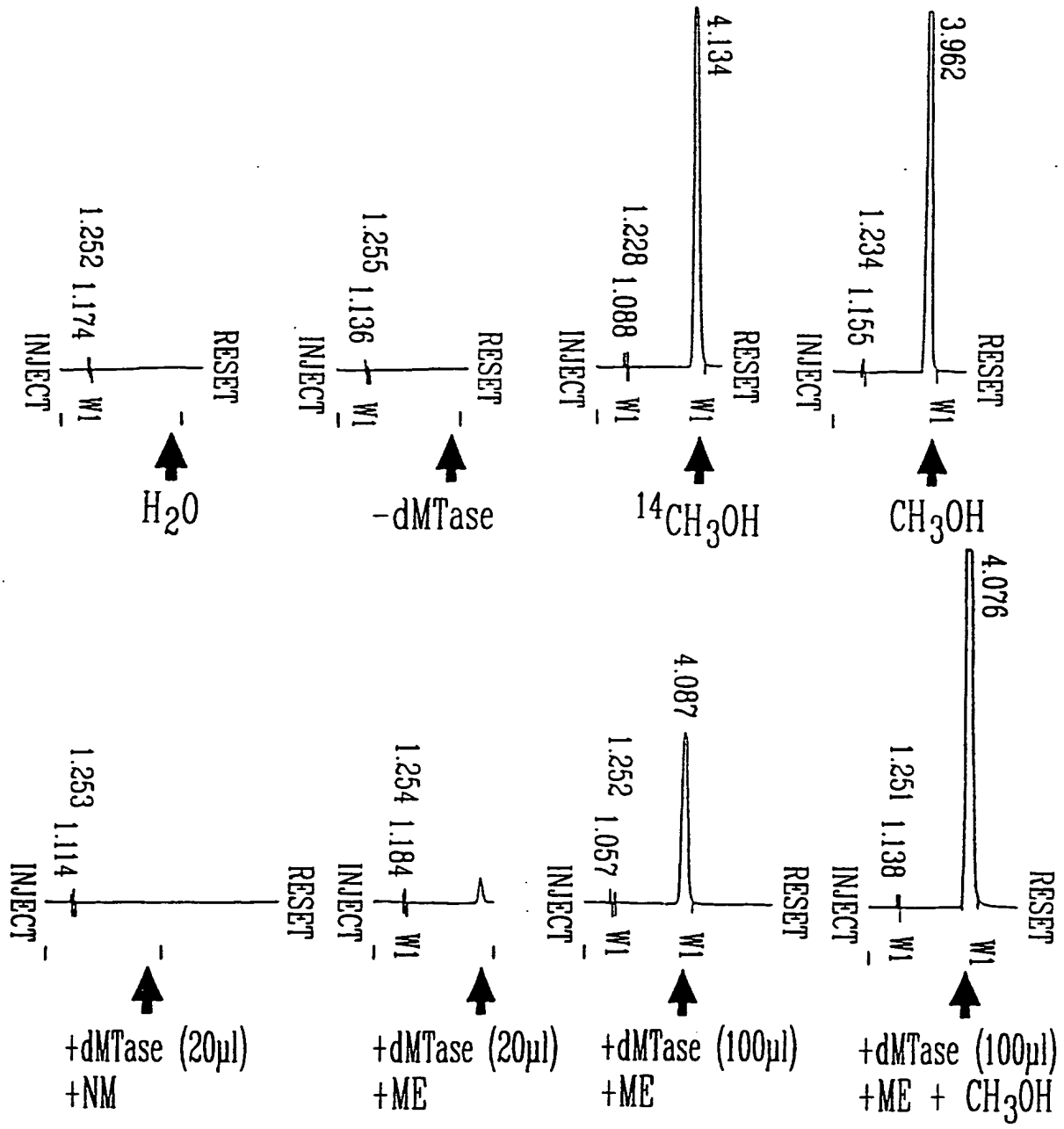

3.962
1.234
1.155
INJECT
W1
RESET
CH3OH
4.134
1.228
1.088
INJECT
W1
RESET
14CH3OH
1.255
1.136
INJECT
W1
RESET
-dMTase
1.252
1.174
INJECT
W1
RESET
H2O
4.076
1.251
1.138
INJECT
W1
RESET
+dMTase (100µl)
+ME + CH3OH
4.087
1.252
1.057
INJECT
W1
RESET
+dMTase (100µl)
+ME
1.254
1.184
INJECT
W1
RESET
+dMTase (20µl)
+ME
1.253
1.114
INJECT
RESET
+dMTase (20µl)
+NM

FIG 4E

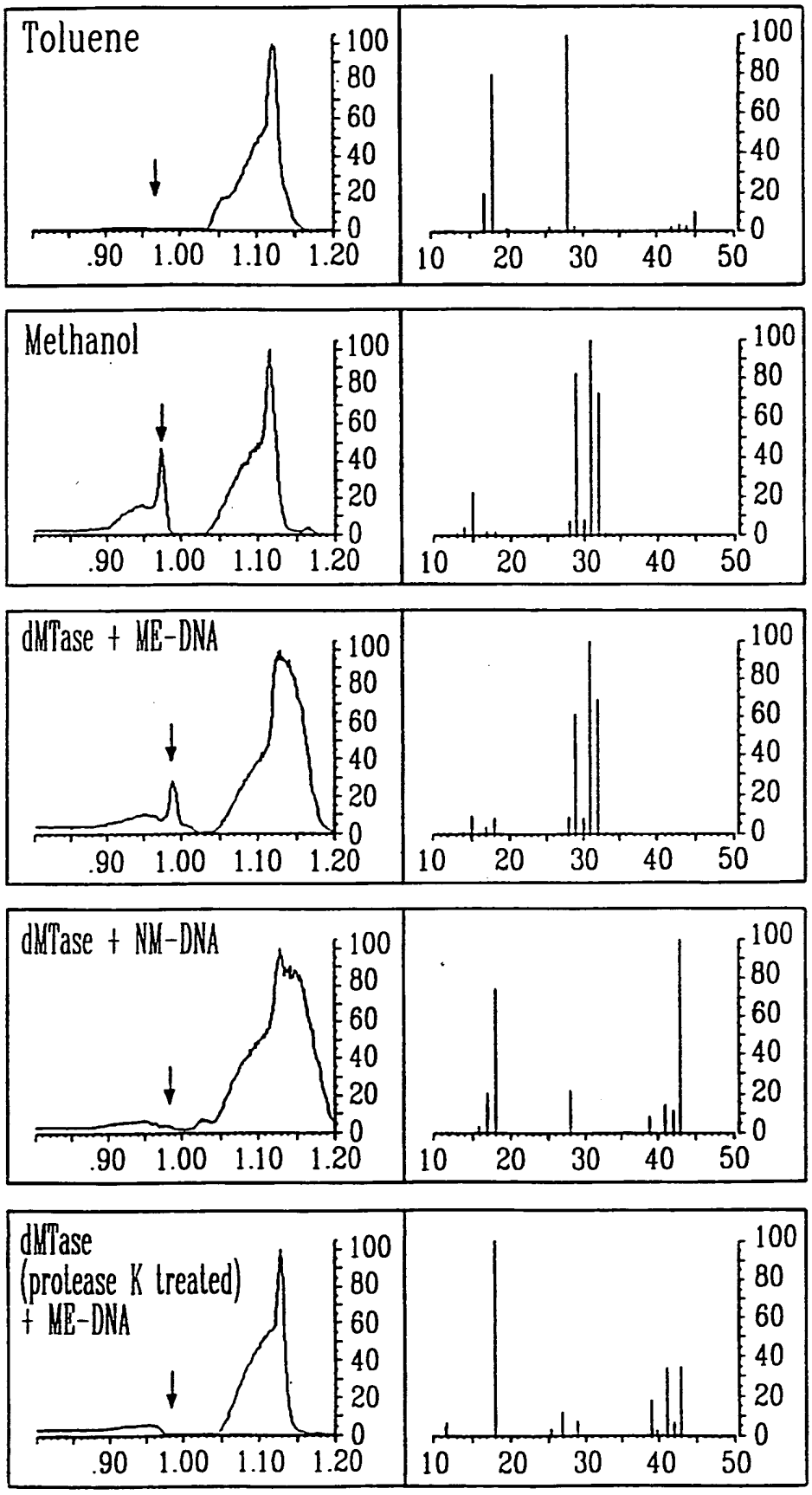
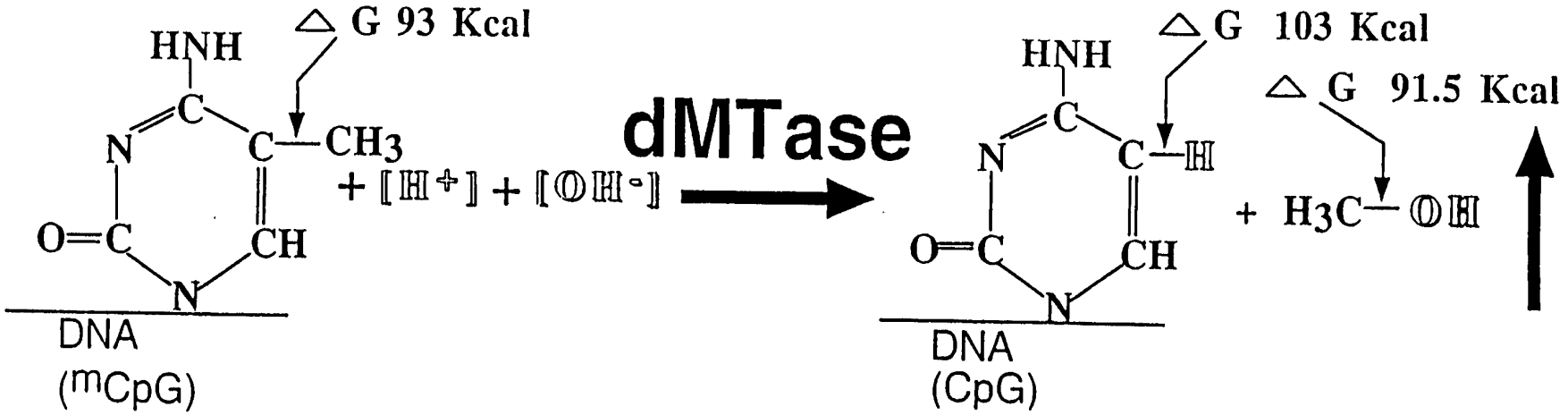

Toluene
Methanol
dMTase + ME-DNA
dMTase + NM-DNA
dMTase
(protease K treated)
+ ME-DNA
.90 1.00 1.10 1.20
10 20 30 40 50
0 20 40 60 80 100

Fig 4F



$$\triangle G_{Reaction} = (93) - (103 + 91.5) = (-101.5)\ Kcal$$

Fig. 5

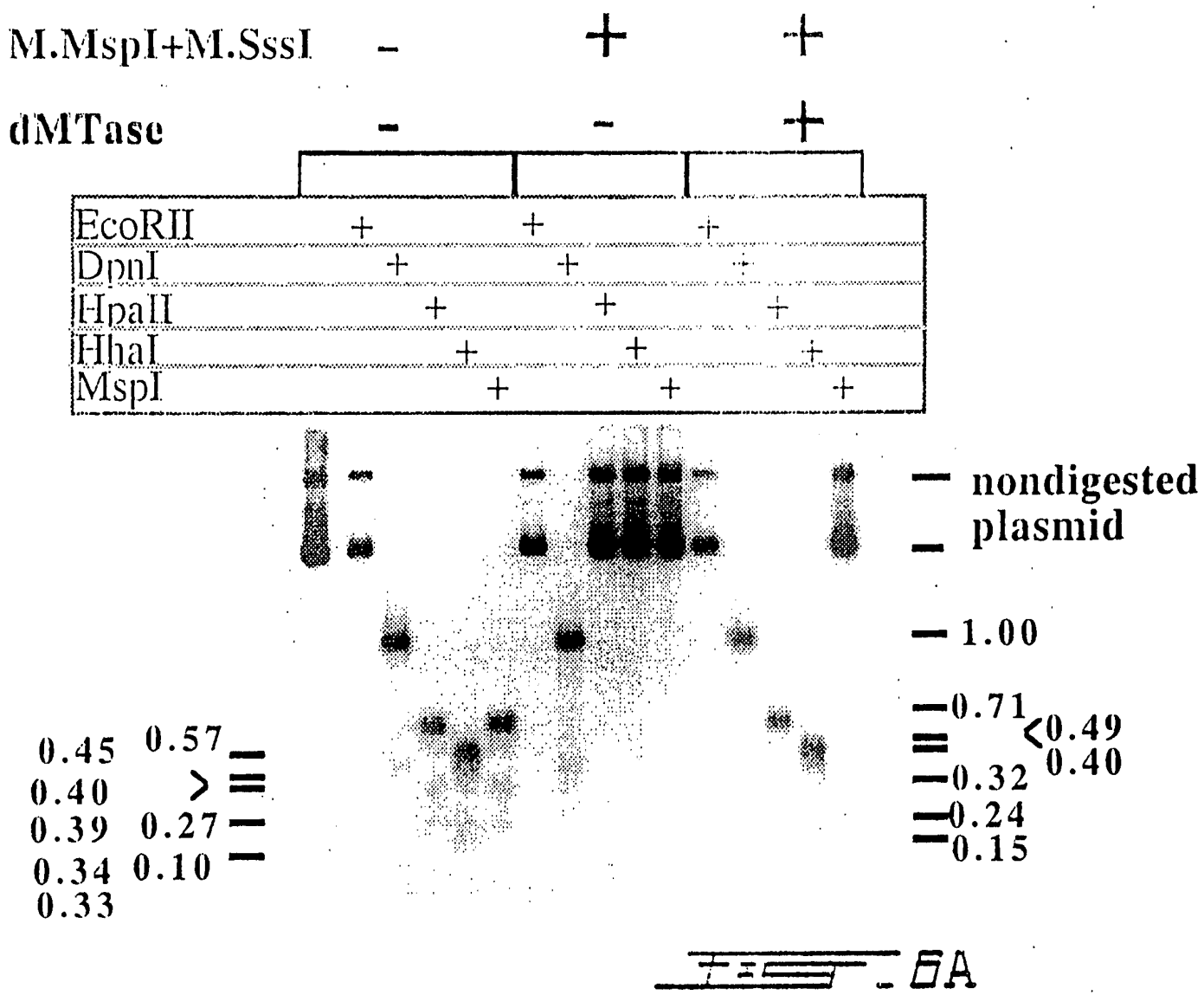


FIG. 6A

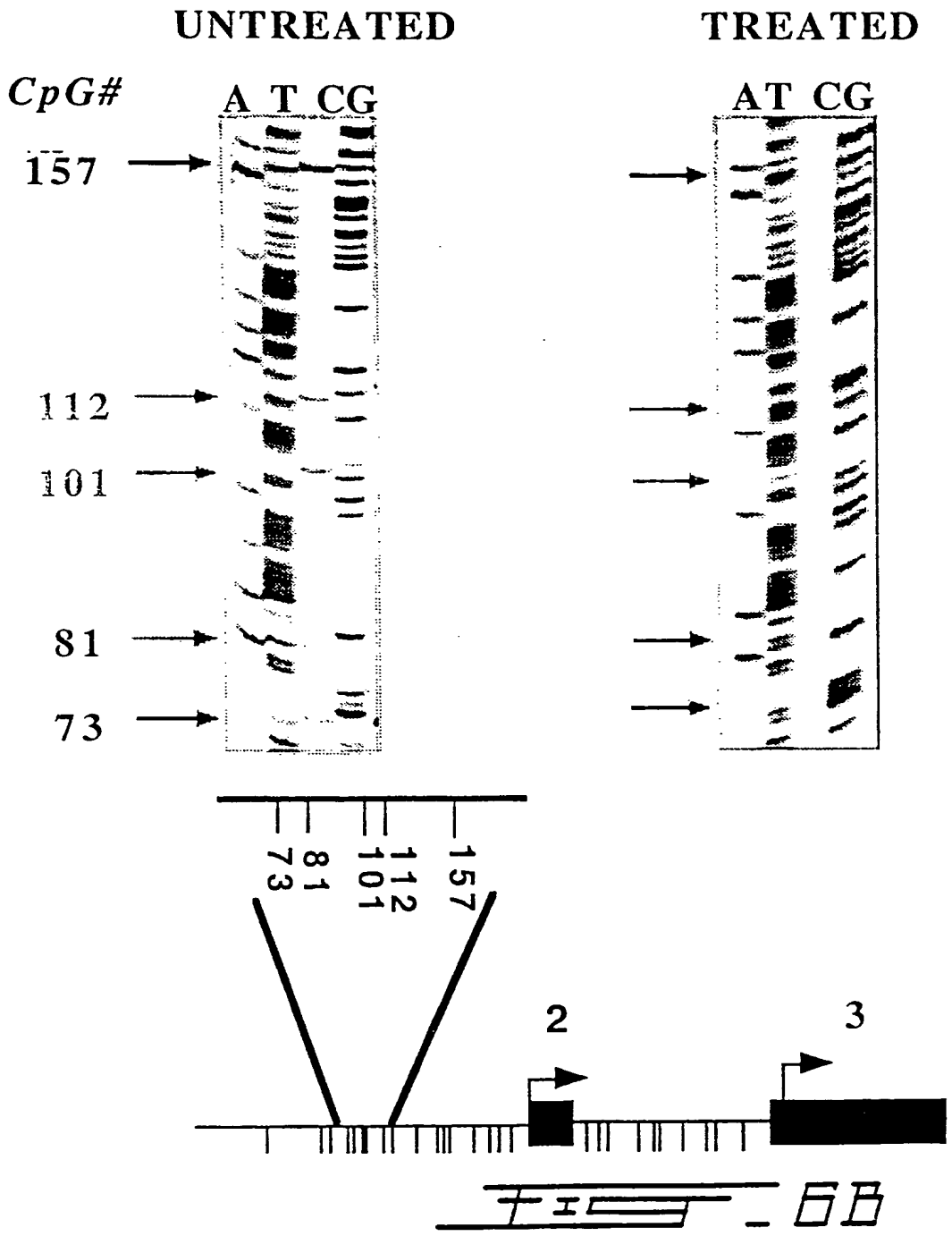


FIG 6B

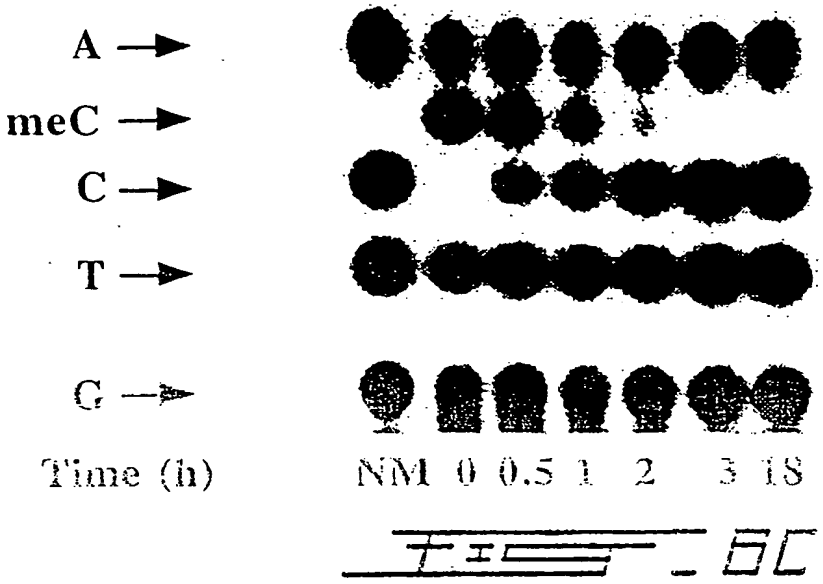

A
meC
C
T
G
Time (h)
NM 0 0.5 1 2 3 18

FIG 6C


HM Control
-RNase
+RNase
Control
CpT
Control
CpA
CpG
ME
NM
mdCMP
dCMP

FIG 6D

FIG. 7A

DNA
CELL
200
116
97
66
44
32.5
21.5

FIG. 7B

Complex 150
MW (kDa)
200
116
97
66
44
32.5
column fraction
61 62 63 64 65
mdCMP
dCMP

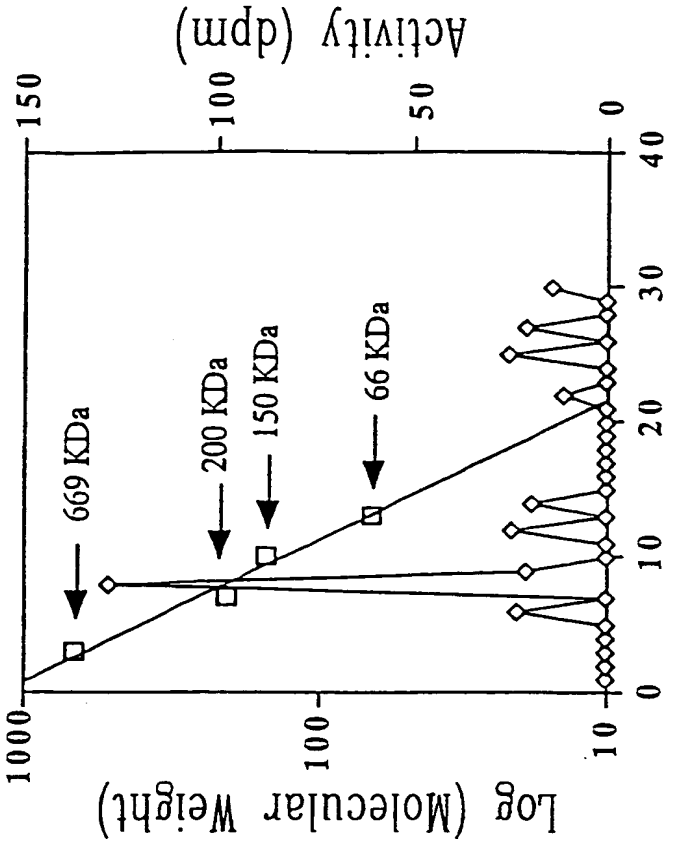


FIG - 7D

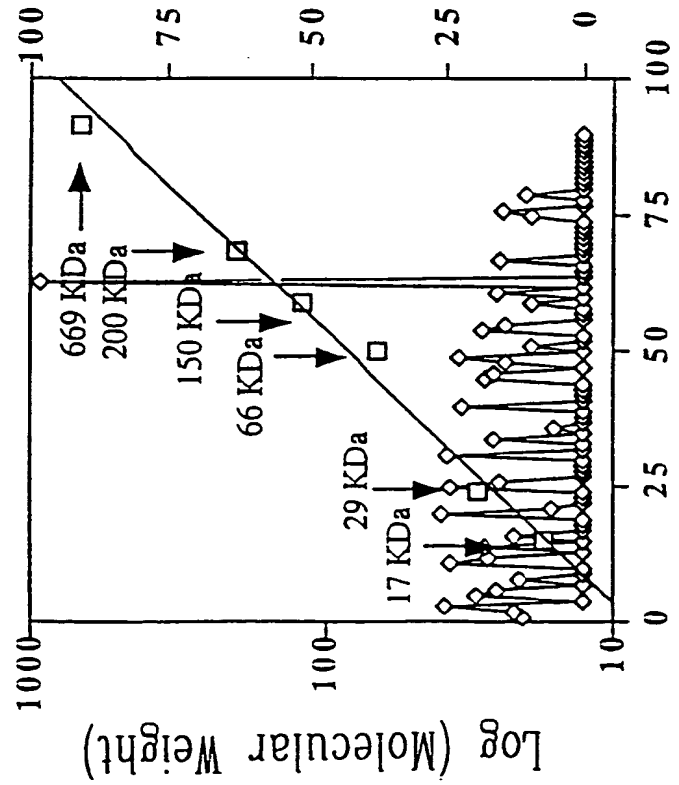


FIG - 7C

```
EST     DCPALPPGWKKEEVIRKSGLSAGKSDVYYFSPSGKKFRSKPQLARYLGNIVDLS
        | | || ||      |||| |||| ||| | || |||| | | |  | |
        D P LP GW ++   RKSG SAGK DVY +P GK FRSK +L Y  D S
        | | || ||      |||| |||| ||| | || |||| | | |  | |
MeCP2   15 DDPTLPEGWIRKLKQRKSGRSAGKYDVYLINPQGKAFRSKVELIAYFEKVGDTS 68
```

FIG 8A

```
MDCPALPPGW KKEEVIRKSG LSAGKSDVYY FSPSGKKFRS 40
KPQLARYLGN TVDLSSFDFR TGKMMPSKLQ KNKQRLRNDP 80
LNQNKGKPDL NTTLPIRQTA SIFKQPVTKV TNHPSNKVKS 120
DPQRMNEQPR QLFWEKRLQG LSASDVTEQI IKTMELPKGL 160
QGVGPGSNDE TLLSAVASAL HTSSAPITGQ VSAAVEKNPA 200
VWLNTSQPLC KAFIVTDEDI RKQEERVQQV RKILEDALMA 240
DILSRAADTE EMDIEMDSGD EA 262
```

homology to methylated DNA binding domain

homology to coiled coil domain

FIG 8B

PCT/CA98/01059

09/554414

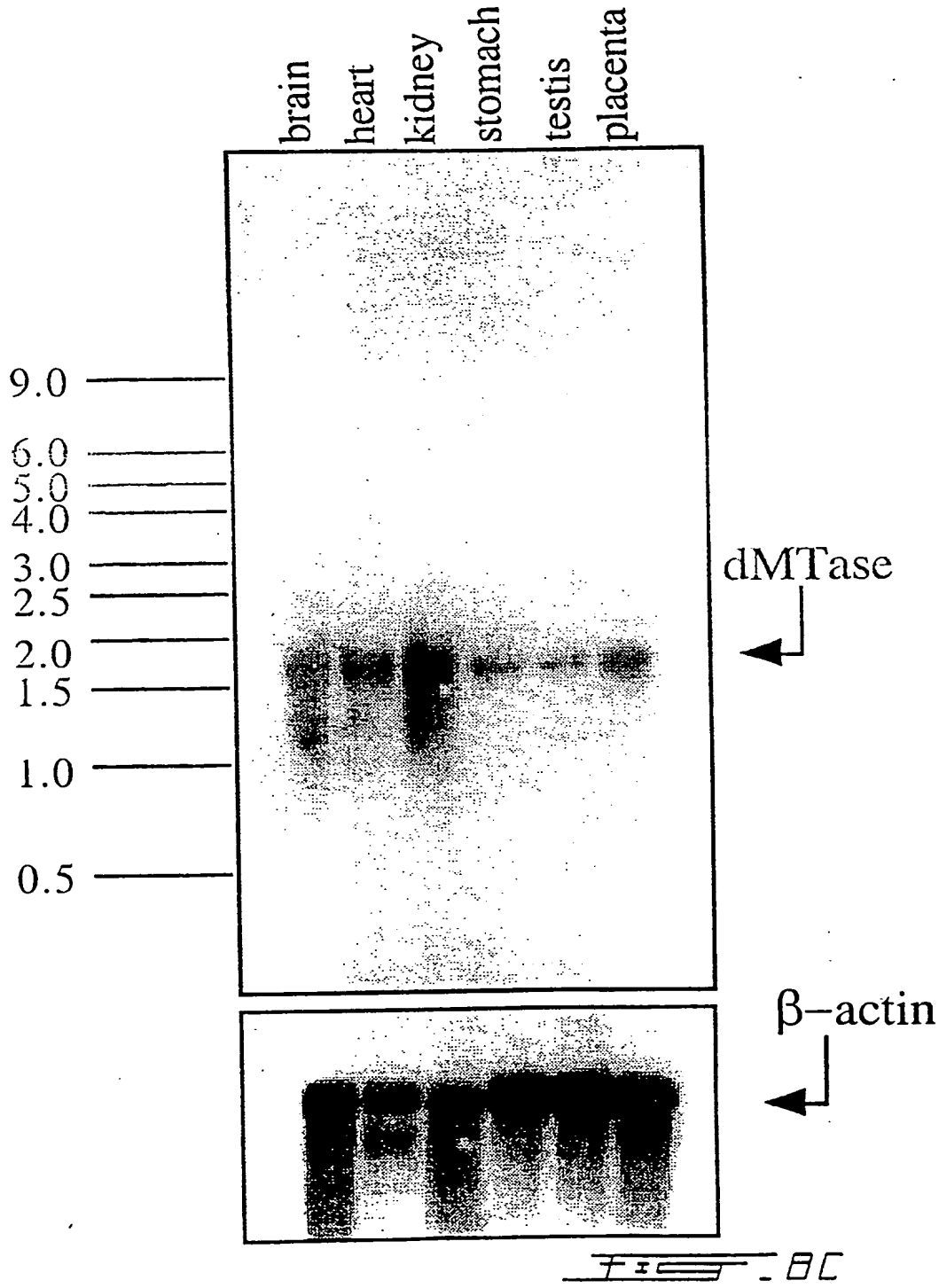

brain
heart
kidney
stomach
testis
placenta
9.0
6.0
5.0
4.0
3.0
2.5
2.0
1.5
1.0
0.5
dMTase
β–actin

Fig. 8C

Human DNA demethylase cDNA-dMTase1 and predicted amino acid sequence

```
5'gggggcgtgg ccccgagaag gcggagacaa gatggccgcc catagcgctt ggaggaccta
  agaggcggtg gccggggcca cgccccgggc aggagggccg ctctgtgcgc gcccgctcta
  tgatgcttgc gcgcgtcccc cgcgcgccgc gctgcgggcg gggcgggtct ccgggattcc
  aagggctcgg ttacggaaga agcgcagcgc cggctgggga gggggctgga tgcgcgcgca
  cccgggggga ggccgctgct gcccggagca ggaggagggg gagagtgcgg cgggcggcag
  cggcgctggc ggcgactccg ccatagagca gggggccag ggcagcgcgc tcgccccgtc
  cccggtgagc ggcgtgcgca gggaaggcgc tcggggcggc ggccgtggcc gggggcggtg
  gaagcaggcg ggccggggcg gcggcgtctg tggccgtggc cggggccggg gccgtggccg
  gggacgggga cggggccggg gccggggccg cggccgtccc ccgagtggcg gcagcggcct
  tggcggcgac ggcggcggct gcggcggcgg cggcagcggt ggcggcggcg ccccccggcg
  ggagccggtc cctttcccgt cggggagcgc ggggccgggg cccaggggac cccgggccac
  ggagagcggg aagaggatgg attgcccggc cctcccccc ggatggaaga aggaggaagt
  gatccgaaaa tctgggctaa gtgctggcaa gagcgatgtc tactacttca gtccaagtgg
  taagaagttc agaagcaagc ctcagttggc aaggtacctg ggaaatactg ttgatctcag
  cagttttgac ttcagaactg gaaagatgat gcctagtaaa ttacagaaga acaaacagag
  actgcgaaac gatcctctca atcaaaataa gggtaaacca gacttgaata caacattgcc
  aattagacaa acagcatcaa ttttcaaaca accggtaacc aaagtcacaa atcatcctag
```

FIG. 9A

taataaagtg aaatcagacc cacaacgaat gaatgaacag ccacgtcagc ttttctggga
gaagaggcta caaggactta gtgcatcaga tgtaacagaa caaattataa aaaccatgga
actacccaaa ggtcttcaag gagttggtcc aggtagcaat gatgagaccc ttttatctgc
tgttgccagt gctttgcaca caagctctgc gccaatcaca gggcaagtct ccgctgctgt
ggaaaagaac cctgctgttt ggcttaacac atctcaaccc ctctgcaaag cttttattgt
cacagatgaa gacatcagga aacaggaaga gcgagtacag caagtacgca agaaattgga
agaagcactg atggcagaca tcttgtcgcg agctgctgat acagaagaga tggatattga
aatggacagt ggagatgaag cctaagaata tgatcaggta actttcgacc gactttcccc
aagrgaaaat tcctagaaat tgaacaaaaa tgtttccact ggcttttgcc tgtaagaaaa
aaaatgtacc cgagcacata gagcttttta atagcactaa ccaatgcctt tttagatgta
tttttgatgt atatatctat tattcaaaaa atcatgttta ttttgagtcc taggacttaa
aattagtctt ttgtaatatc aagcaggacc ctaagatgaa gctgagcttt tgatgccagg
tgcaatctac tggaaatgta gcacttacgt aaaacatttg tttcccccac agttttaata
agaacagatc aggaattcta aataaatttc ccagttaaag attattgtga cttcactgta
tataaacata tttttatact ttattgaaag gggacacctg tacattcttc catcatcact
gtaaagacaa ataaatgatt atattcacaa aaaaaaaaaa aaaaaa 3'

SEQ ID NO:1

Fig 9B

MRAHPGGGRCCPEQEEGESAAGGSGAGGDSAIEQGGQGSALAPSPVSGVR
REGARGGGRGRGRWKQAGRGGGVCGRGRGRGRGRGRGRGRGRGRPPSG
GSGLGGDGGGCGGGGSGGGGAPRREPVPFPSGSAGPGPRGPRATESGKRM
DCPALPPGWKKEEVIRKSGLSAGKSDVYYFSPSGKKFRSKPQLARYLGNT
VDLSSFDFRTGKMMPSKLQKNKQRLRNDPLNQNKGKPDLNTTLPIRQTAS
IFKQPVTKVTNHPSNKVKSDPQRMNEQPRQLFWEKRLQGLSASDVTEQII
KTMELPKGLQGVGPGSNDETLLSAVASALHTSSAPITGQVSAAVEKNPAV
WLNTSQPLCKAFIVTDEDIRKQEERVQQVRKKLEEALMADILSRAADTEE
MDIEMDSGDEA

SEQ ID NO:2

Fig 9C

Human DNA demethylase homologue-dMTase2 and predicted amino acid sequence

5'agcgggccga ggagccgggc gcaatggagc ggaagaggtg ggagtgcccg gcgctcccgc
agggctggga gagggaagaa gtgcccagaa ggtcggggct gtcggccggc cacagggatg
tcttttacta tagcccgagc gggaagaagt tccgcagcaa gccgcagctg gcgcgctacc
tgggcggctc catggacctg agcaccttcg acttccgcac gggcaagatg ctgatgagca
agatgaacaa gagccgccag cgcgtgcgct acgactcctc caaccaggtc aagggcaagc
ccgacctgaa cacggcgctg cccgtgcgcc agacggcgtc catcttcaag cagccggtga
ccaagattac caaccacccc agcaacaagg tcaagagcga cccgcagaag gcggtggacc
agccgcgcca gctcttctgg gagaagaagc tgagcggcct gaacgccttc gacattgctg
aggagctggt caagaccatg gacctcccca agggcctgca gggggtggga cctggctgca
cggatgagac gctgctgtcg gccatcgcca gcgccctgca cactagcacc atgcccatca
cgggacagct ctcggccgcc gtggagaaga accccggcgt atggctcaac accacgcagc
ccctgtgcaa agccttcatg gtgaccgacg aggacatcag gaagcaggaa gagctggtgc
agcaggtgcg gaagcggctg gaggaggcgc tgatggccga catgctggcg cacgtggagg
agctggcccg tgacggggag gcgccgctgg acaaggcctg cgctgaggac gacgacgagg
aagacgagga ggaggaggag gaggagcccg acccggaccc ggagatggag cacgtctagg
gcagaggccc tgccgagagc ccgtgctgcc tgctggagcc gcctgcagac gcggtcctcg
gccccacgtg aaccaggctc ggcggcgaag cccagccttg gagacaccca ggaggaaggc
cgtgctcctg gctccctcct cggcccgtcc ccacttcccg gggcctcggg gcacacagct
ggggctgccc ccacccgaaa gaccctccac gctcgtcctc tacagagtcc ggcttcggga
agtgccgggt gctcctgggc cctgcctggc tccctacgac ctttgggctc gaggccagct

Fig-90

cctccccatg cccgctgtcc cagctccttg agactggaga gcagccagca ggtgcccggc
agctcggcgc cacggcttgc tgacagctgg gagggtttct cggtctggag gcgtagtttt
gaaactcaca tcacccactg tgcagcgtga ggacgggact ctggtctgct gtgggggca
tgcaggacgg cgccactctc tgccctgcca tgcggctggt ggtgccacag agcctcaccg
tgcctgagtg gcgtgcccag ggaggccgct ctccttcagt aaatgtaaca cagtcgaggc
acgtcatcgg gcagccttcc ctgtgtgcca acgccagcct tcgcttctga aaaccaaact
ccagccgctg ccagtcggga cttggtcgcc cggcgctgcc agaatgctcc actgccagcc
ggcccccctg cctcggtttc ccttctgttt agtggcgaca caggcaccca gctttggggt
ggtgctgacg ctcccagggg tgccaggagc cactgggaca gggtgaggct cccagacgct
cctcgaggtg cccagctctc cagggagctt ctggcccaag gcgttcttga gggatctgct
ccttaacccc ccagtgcctt ggcgagggca ggttccaagc cacagacgcc tgccccgagt
ggactttgcg gccagtccct gggtgccttc ctgggccctg cttgcccagt gagggttcct
aacgggtggg ttcawtggcc tggcccvagc gagcccccac ctgcattgac cttaggccca
tagagagggc ctgtcccggt gctgccccag ccaaggatct ggtcgctgcc ccaggggac
tgatgggcaa gagtcgcccc tgtggctgga ctgtgaccat ccctgatggg gcctgaccgc
gggagctgag gaagcgccgc tccaccgtct gccctccaag gacccgcatg gaggcagtgg
gctggcagct tcctgctgct ccctgtcaga gtcaaagcac aaatcctcag gacgggctca
agggccaggg cagccgaggg aagctccagg tggggaccac gtcttcctga ggttggtgcc
cactggctgg gaccctttgc agtggggtgg cctcccctct gtctgcctgg tggagggagc
cgtgggcgtg gggacgtgac tgaataaagc caccatgggt ggatgtgctt gg 3'

SEQ ID NO:3

FIG 9E

MERKRWECPALPQGWEREEVPRRSGLSAGHRDVFYYSPSGKKFRSKPQLA
RYLGGSMDLSTFDFRTGKMLMSKMNKSRQRVRYDSSNQVKGKPDLNTALP
VRQTASIFKQPVTKITNHPSNKVKSDPQKAVDQPRQLFWEKKLSGLNAFD
IAEELVKTMDLPKGLQGVGPGCTDETLLSAIASALHTSTMPITGQLSAAV
EKNPGVWLNTTQPLCKAFMVTDEDIRKQEELVQQVRKRLEEALMADMLAH
VEELARDGEAPLDKACAEDDDEEDEEEEEEEPDPDPEMEHV

SEQ ID NO:4

FIG. 9F

Lipman-Pearson Protein Alignment

Ktuple: 2; Gap Penalty: 4; Gap Length Penalty: 12

Seq1(1>411)	Seq2(1>291)	Similarity	Gap	Gap	Consensus
human dMTase1 protein	human dMTase2 protein	Index	Number	Length	Length
(148>397)	(4>253)	76.0	0	0	250
(148>397)	(4>253)	76.0	0	0	250

```
  v150      v160      v170      v180      v190      v200      v210
KRMDCPALPPGWKKEEVIRKSGLSAGKSDVYYFSPSGKKFRSKPQLARYLGNTVDLSSFDFRTGKMMPSK
KR :CPALP.GW.:EEV R:SGLSAG..DV:Y:SPSGKKFRSKPQLARYLG.::DLS:FDFRTGKM: SK
KRWECPALPQGWEREEVPRRSGLSAGHRDVFYYSPSGKKFRSKPQLARYLGGSMDLSTFDFRTGKMLMSK
        ^10       ^20       ^30       ^40       ^50       ^60       ^70

   v220      v230      v240      v250      v260      v270      v280
LQKNKQRLRNDPLNQNKGKPDLNTTLPIRQTASIFKQPVTKVTNHPSNKVKSDPQRMNEQPRQLFWEKRL
::K::QR:R D: NQ KGKPDLNT:LP:RQTASIFKQPVTK:TNHPSNKVKSDPQ:  :QPRQLFWEK:L
MNKSRQRVRYDSSNQVKGKPDLNTALPVRQTASIFKQPVTKITNHPSNKVKSDPQKAVDQPRQLFWEKKL
        ^80       ^90      ^100      ^110      ^120      ^130      ^140
```

FIG. 9G

```
  v290       v300       v310       v320       v330       v340       v350
QGLSASDVTEQIIKIMELPKGLQGVGPGSNDETLLSAVASALHTSSAPITGQVSAAVEKNPAVWLNISQP
 GL:A D::E:::KIM:LPKGLQGVGPG..DETLLSA:ASALHTS: PITGQ:SAAVEKNP:VWLNT:QP
SGLNAFDIAEELVKIMDLPKGLQGVGPGCTDETLLSAIASALHTSTMPITGQLSAAVEKNPGVWLNITQP
      ^150       ^160       ^170       ^180       ^190       ^200       ^210

  v360       v370       v380       v390
LCKAFIVTDEDIRKQEERVQQVRKKLEEALMADILSRAAD
LCKAF:VTDEDIRKQEE VQQVRK:LEEALMAD:L::..:
LCKAFMVTDEDIRKQEELVQQVRKRLEEALMADMLAHVEE
      ^220       ^230       ^240       ^250
```

Fig 9H

Mouse DNA demethylase-dMTase1 and predicted amino acid sequence

```
5'ccgctctgcg ggcggggcgg gtctccggga ttccaagggc tcggttacgg aagaagcgca
  gagccggctg gggagggggc tggatgcgcg cgcacccggg gggaggccgc tgctgcccgg
  agcaggagga gggggagagc gcggcgggcg gcagcggcgc tggcggcgac tccgccatag
  agcagggggg ccagggcagc gcgctcgctc cgtccccggt gagcggcgtg cgcagggaag
  gcgctcgggg cggcggccgt ggccgggggc ggtggaagca ggcggcccgg ggcggcggcg
  tctgtggccg tggccgtggc cgtggccggg gtcggggccg tggccggggc cggggccggg
  gccgcggccg tccccagagt ggcggcagcg gccttggcgg cgacggcggc ggcggcgcgg
  gcggctgcgg cgtcggcagc ggtggcggcg tcgccccccg gcgggatcct gtccctttcc
  cgtcggggag ctcggggccg gggcccaggg gaccccgggc cacggagagc gggaagagga
  tggactgccc ggccctcccc cccggatgga agaaggagga agtgatccga aaatcagggc
  tcagtgctgg caagagcgat gtctactact tcagtccaag tggtaagaag ttcagaagta
  aacctcagct ggcaagatac ctgggaaatg ctgttgacct tagcagtttt gacttcagga
  ccggcaagat gatgcctagt aaattacaga agaacaagca gagactccgg aatgacccccc
  tcaatcagaa caagggtaaa ccagacctga acacaacatt gccaattaga caaactgcat
  caatttcaa gcaaccagta accaaattca cgaaccaccc gagcaataag gtgaagtcag
  acccccagcg gatgaatgaa caaccacgtc agcttttctg ggagaagagg ctacaaggac
  ttagcgcatc agatgtaaca gaacaaatta taaaaaccat ggagctacct aaaggtcttc
  aaggagtcgg tccaggtagc aatgacgaga cccttctgtc tgctgtggcc agtgctttac
```

Fig. 9I

acacaagctc tgcgcccatc acaggacaag tctctgctgc cgtggaaaag aaccctgctg
tttggcttaa cacatctcaa cccctctgca aagctttcat tgttacagat gaagacatta
ggaaacagga agagcgagtc caacaagtac gcaagaaact ggaggaggca ctgatggccg
acatcctgtc ccgggctgcg gacacggagg aagtagacat tgacatggac agtggagatg
aggcgtaaga atatgatcag gtaactttcg actgaccttc cccaagagca aattgctaga
aacagaatta aaacatttcc actgggtttc gcctgtaaga aaaagtgtac ctgagcacat
agcttttaa tagcactaac caatgccttt ttagatgtat ttttgatgta tatatctatt
attccaaatg atgtttattt tgaatcctag gacttaaaat gagtctttta taatagcaag
cagggccctt ccggtgcagt gcagctttga ggccaggtgc agtctactgg aaaggtagca
cttacgtgaa atatttgttt cccccacagt tttaatataa acagatcagg agtaccaaat
aagtttccca attaaagatt attatacttc actgtatata aacagatttt tatactttat
tgaaagaaga tacctgtaca ttcttccatc atcactgtaa agacaaataa atgactatat
tcac 3′

SEQ ID NO:5

FIG. 9J

MRAHPGGGRCCPEQEEGESAAGGSGAGGDSAIEQGGQGSALAPSPVSGVR
REGARGGGRGRGRWKQAARGGGVCGRGRGRGRGRGRGRGRGRGRPQSG
GSGLGGDGGGGAGGCGVGSGGGVAPRRDPVPFPSGSSGPGPRGPRATESG
KRMDCPALPPGWKKEEVIRKSGLSAGKSDVYYFSPSGKKFRSKPQLARYL
GNAVDLSSFDFRTGKMMPSKLQKNKQRLRNDPLNQNKGKPDLNTTLPIRQ
TASIFKQPVTKFTNHPSNKVKSDPQRMNEQPRQLFWEKRLQGLSASDVTE
QIIKTMELPKGLQGVGPGSNDETLLSAVASALHTSSAPITGQVSAAVEKN
PAVWLNTSQPLCKAFIVTDEDIRKQEERVQQVRKKLEEALMADILSRAAD
TEEVDIDMDSGDEA

SEQ ID NO:6

Fig 9K

PCT/CA98/01059

Mouse DNA demethylase-dMTase2 and predicted amino acid sequence

```
5'cacgcgcggg cgggtgggcg gagcggcccc cctagcgggg gctgtgaagc gcggggaggg
  ggccgagcgg gtggcgaagc cggcgcgcgc ccggctgggg gcggagggcg gaggcccgtg
  ggacagaaca gctgcggcga gtggcggcgg cggagggagc cgaatcggcg acgagcccgg
  gggtcgcaac ttgcagaagc ggcggcggcg gcggcatcgg ccacggcggg cggaaaagcc
  ggggcgcaat ggagcggaag aggtgggagt gcccggcgct cccgcagggc tgggaaaggg
  aagaagtgcc caggaggtcg gggctgtcgg ccggccacag ggatgtcttt tactatagcc
  ccagcgggaa gaagttccgc agcaagccac aactggcacg ttacctgggc ggatccatgg
  acctcagcac cttcgacttc cgcaccggaa agatgttgat gaacaagatg aataagagtc
  gccagcgtgt gcgctatgat tcttccaacc aggtcaaggg caagcctgac ctgaacaccg
  cgctgcctgt acggcagact gcatccatct tcaagcaacc ggtgaccaag atcaccaacc
  accccagcaa caaggtcaag agcgacccgc agaaggcagt ggaccagccg aggcagcttt
  tctgggagaa gaagctaagt ggattgagtg cctttgacat tgcagaagaa ctggtcagga
  ccatggactt gcccaagggc ctgcagggag tgggccctgg ctgtacagat gagacgctgc
  tgtcagccat tgcgagtgct ctacacacca gcaccctgcc cattacaggc cagctctctg
  cagccgtgga gaagaaccct ggtgtgtggc tgaacactgc acagccactg tgcaaagcct
  tcatggtgac agatgacgac atcaggaagc aggaggagct ggtacagcag gtacggaagc
  gcctggagga ggcactgatg gccgacatgc tagctcatgt ggaggagctt gcccgagacg
  gggaggcacc actggacaag gcctgtgcag aggaggaaga ggaggaggaa gaggaggagg
```

Fig - 9L

```
aagagccgga gccagagcga gtgtagcaca ggtgccctgc ccaagtctgg gctgcagact
gccttcagcc ttgcctggac caggtagggg ccagacctgt aggaggcagc cgtccacctc
ctttccaaag cctcctgctt ccaggtctca gtgcagggag cccctgtgga ccttgaactc
acttgtccct gcgctgcctg gcaggaagcc ccacactgaa agcagatgag cagtgaccca
actgagaggc cacctggaca cagtcacctc cctgcctcct tatcatagga caaggccttg
cttggcaccg aggagctggg agccgtgttg ggtgctggag gaagtttctg gaaacacacc
tggctatgcc caccttatgt ccctaaggct attacaggcc agggtttgga ctgctccggc
ccacagggct gcccagcctc cccacactga gggtcagcag cccaccagga agtcactttc
cttcaataaa ctgatggtag gaacttgtg   3'
```

SEQ ID NO:7

Fig. 9M

FIG - 8N

SEQ ID NO:8

MERKRWECPALPQGWEREEVPRRSGLSAGHRDVFYYSPSGKKFRSKPQLA
RYLGGSMDLSTFDFRTGKMLMNKMNKSRQRVRYDSSNQVKGKPDLNTALP
VRQTASIFKQPVTKITNHPSNKVKSDPQKAVDQPRQLFWEKKLSGLSAFD
IAEELVRTMDLPKGLQGVGPGCTDETLLSAIASALHTSTLPITGQLSAAV
EKNPGVWLNTAQPLCKAFMVTDDDIRKQEELVQQVRKRLEEALMADMLAH
VEELARDGEAPLDKACAEEEEEEEEEEPEPERV

Lipman-Pearson Protein Alignment
Ktuple: 2; Gap Penalty: 4; Gap Length Penalty: 12

Seq1(1>414)	Seq2(1>285)	Similarity	Gap	Gap	Consensus
mouse dMTase1 protein	mouse dMTase2 protein	Index	Number	Length	Length
(151>400)	(4>253)	75.2	0	0	250
(151>400)	(4>253)	75.2	0	0	250

```
         v160       v170       v180       v190       v200       v210       v220
KRMDCPALPPGWKKEEVIRKSGLSAGKSDVYYFSPSGKKFRSKPQLARYLGNAVDLSSFDFRTGKMMPSK
KR :CPALP.GW.:EEV R:SGLSAG..DV:Y:SPSGKKFRSKPQLARYLG.::DLS:FDFRTGKM: :K
KRWECPALPQGWEREEVPRRSGLSAGHRDVFYYSPSGKKFRSKPQLARYLGGSMDLSTFDFRTGKMLMNK
      ^10        ^20        ^30        ^40        ^50        ^60        ^70

         v230       v240       v250       v260       v270       v280       v290
LQKNKQRLRNDPLNQNKGKPDLNITLPIRQTASIFKQPVTKFTNHPSNKVKSDPQRMNEQPRQLFWEKRL
::K::QR:R D: NQ KGKPDLNT:LP:RQTASIFKQPVTK:TNHPSNKVKSDPQ:  :QPRQLFWEK:L
MNKSRQRVRYDSSNQVKGKPDLNTALPVRQTASIFKQPVTKITNHPSNKVKSDPQKAVDQPRQLFWEKKL
      ^80        ^90        ^100       ^110       ^120       ^130       ^140
```

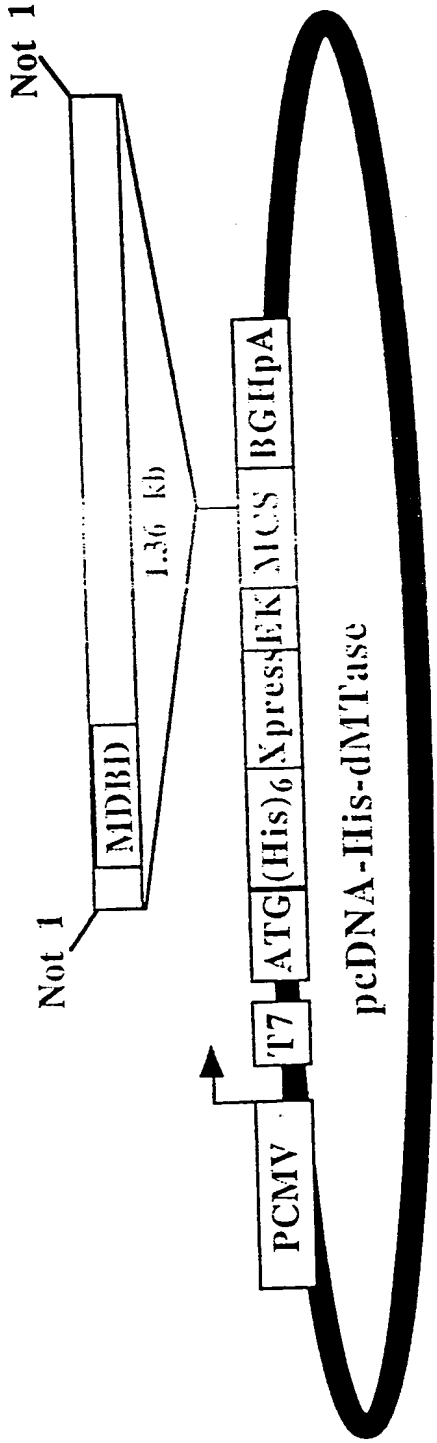
Fig 90

```
          v300       v310       v320       v330       v340       v350       v360
QGLSASDVTEQIIKIMELPKGLQGVGPGSNDETLLSAVASALHTSSAPITGQVSAAVEKNPAVWLNTSQP
 GLSA D::E::::TM:LPKGLQGVGPG..DETLLSA:ASALHTS: PITGQ:SAAVEKNP:VWLNT:QP
SGLSAFDIAEELVRTMDLPKGLQGVGPGCTDETLLSAIASALHTSTLPITGQLSAAVEKNPGVWLNTAQP
      ^150       ^160       ^170       ^180       ^190       ^200       ^210

          v370       v380       v390       v400
LCKAFIVTDEDIRKQEERVQQVRKKLEEALMADILSRAAD
LCKAF:VTD:DIRKQEE VQQVRK:LEEALMAD:L::..:
LCKAFMVTDDDIRKQEELVQQVRKRLEEALMADMLAHVEE
      ^220       ^230       ^240       ^250
```

FIG 9P

09/554414



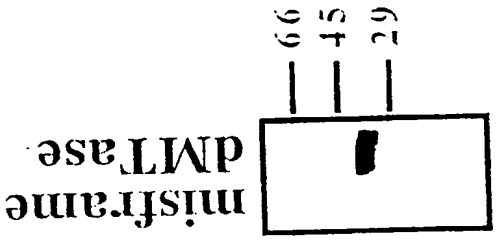


FIG - 10A

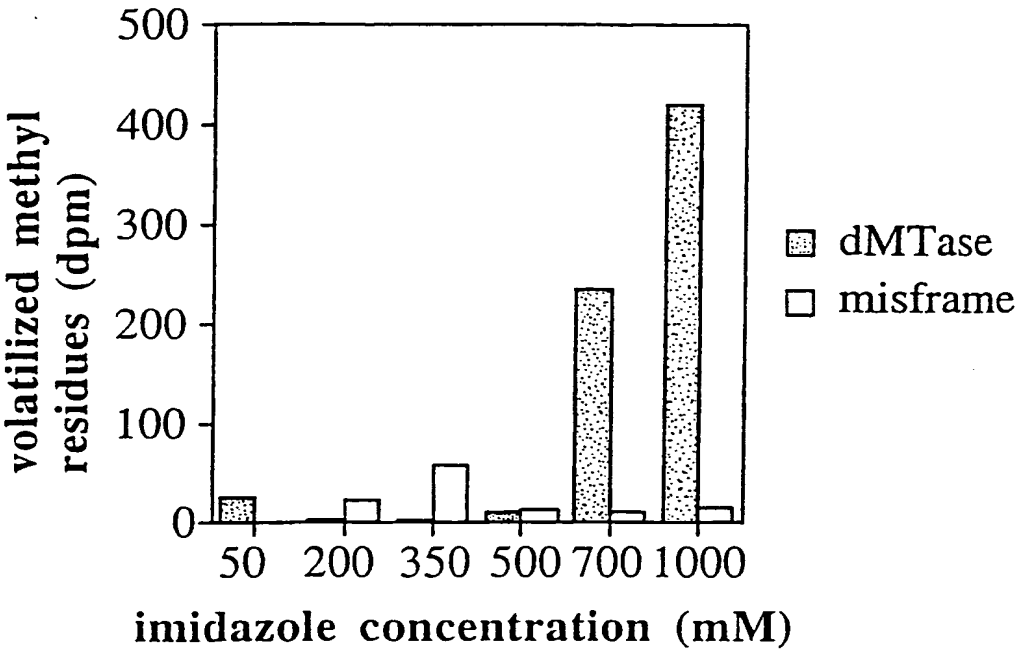

500
400
300
200
100
0
volatilized methyl residues (dpm)
50 200 350 500 700 1000
imidazole concentration (mM)
dMTase
misframe

FIG. 10B

FIG. 10C

FIG. 10B

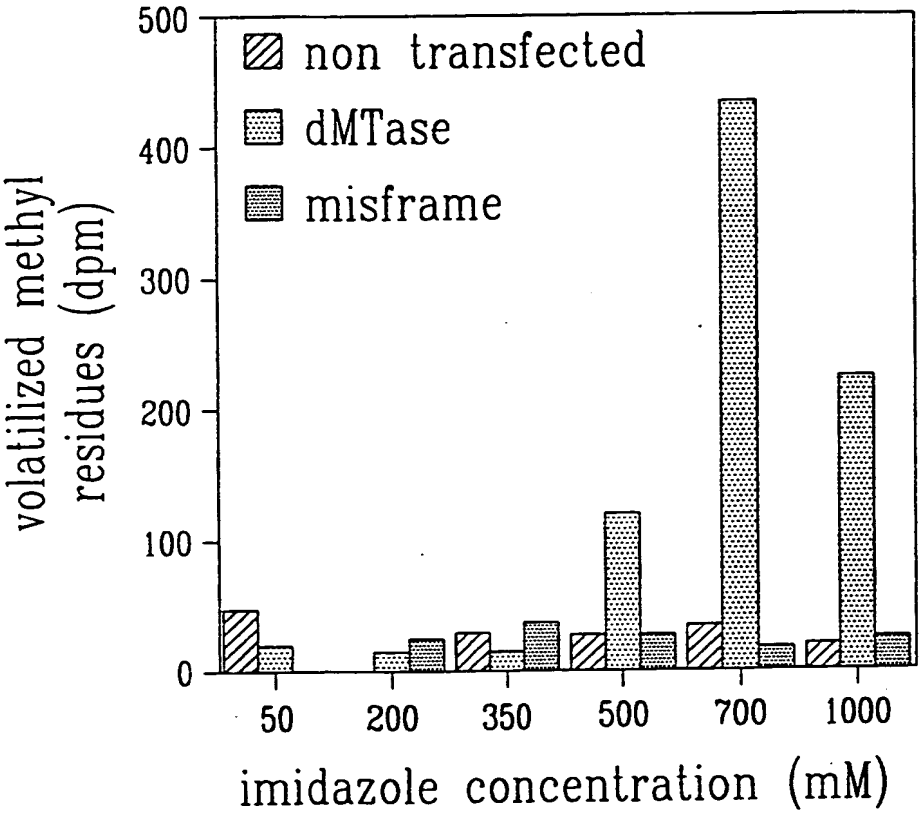

500
400
300
200
100
0
non transfected
dMTase
misframe
volatilized methyl residues (dpm)
50
200
350
500
700
1000
imidazole concentration (mM)

Fig. 11A

FIG. 11E
me SK + Hpa II
0.71
0.49, 0.40
0.32
0.24
0.15
dMTase
Buffer L
dMTase+
Protease K
FIG. 11D
dMTase
NM
ME
mdCMP
dCMP
pBluescript SK+
substrate
(mdCpdG)n
FIG. 11C
dMTase + Protease K
mistrame
dMTase
ME
NM
FIG. 11B
dMTase
empty vector
250
148
60
42
30

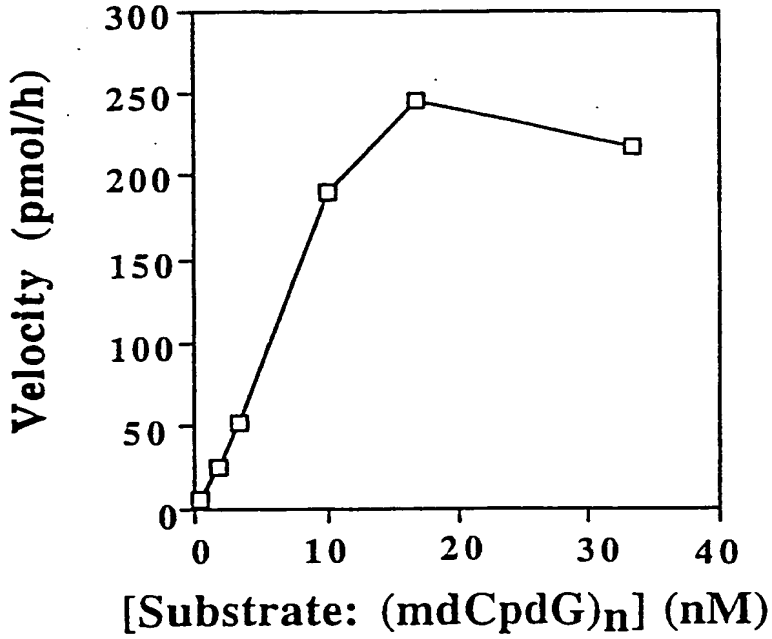

Velocity (pmol/h)
300
250
200
150
100
50
0
0
10
20
30
40
[Substrate: (mdCpdG)n] (nM)

Fig. 11F

FIG-12A

FIG-12B

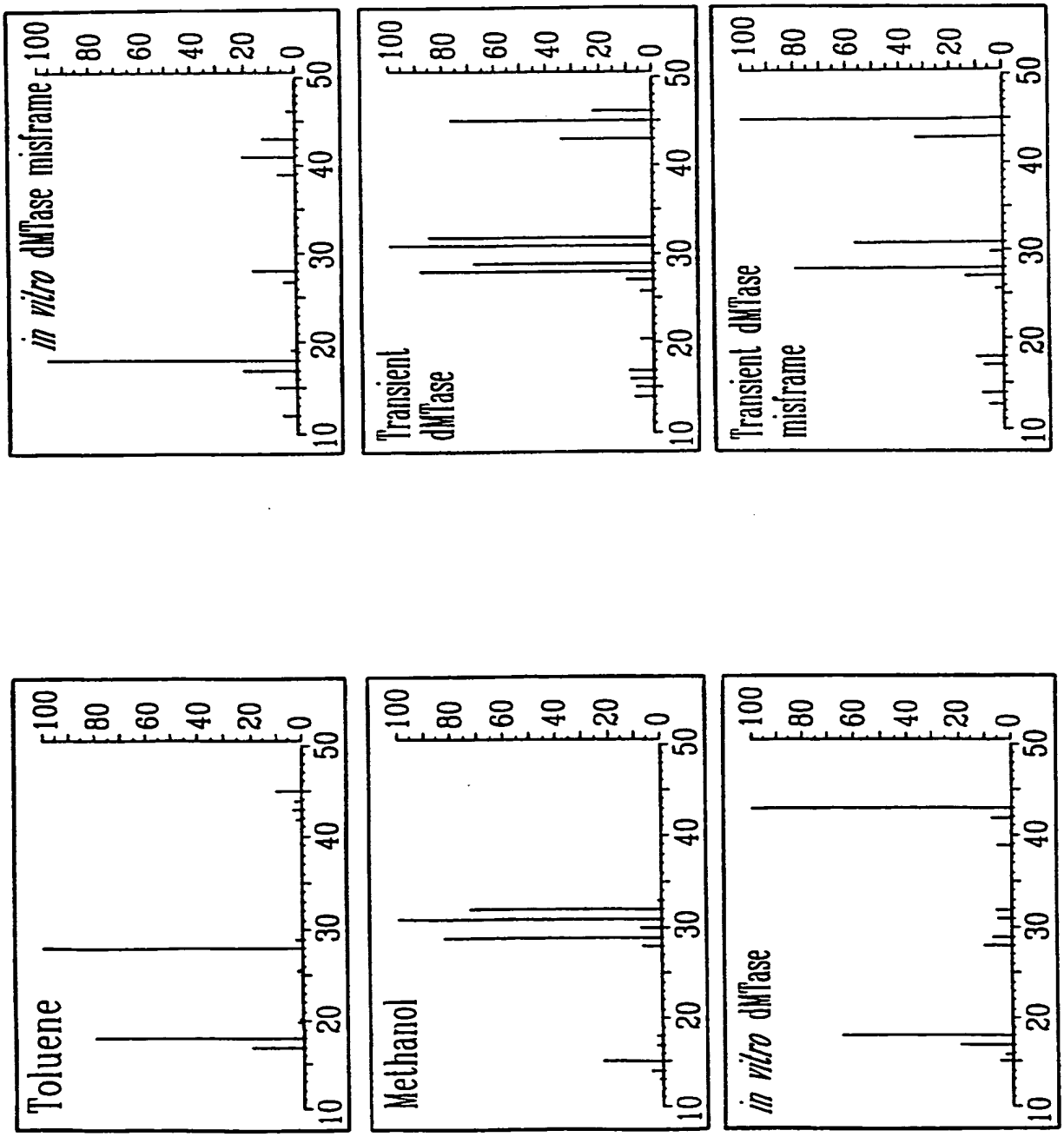

in vitro dMTase misframe
Transient dMTase
Transient dMTase misframe
Toluene
Methanol
in vitro dMTase
100
80
60
40
20
0
10
20
30
40
50

Fig-13A

Fig-13B

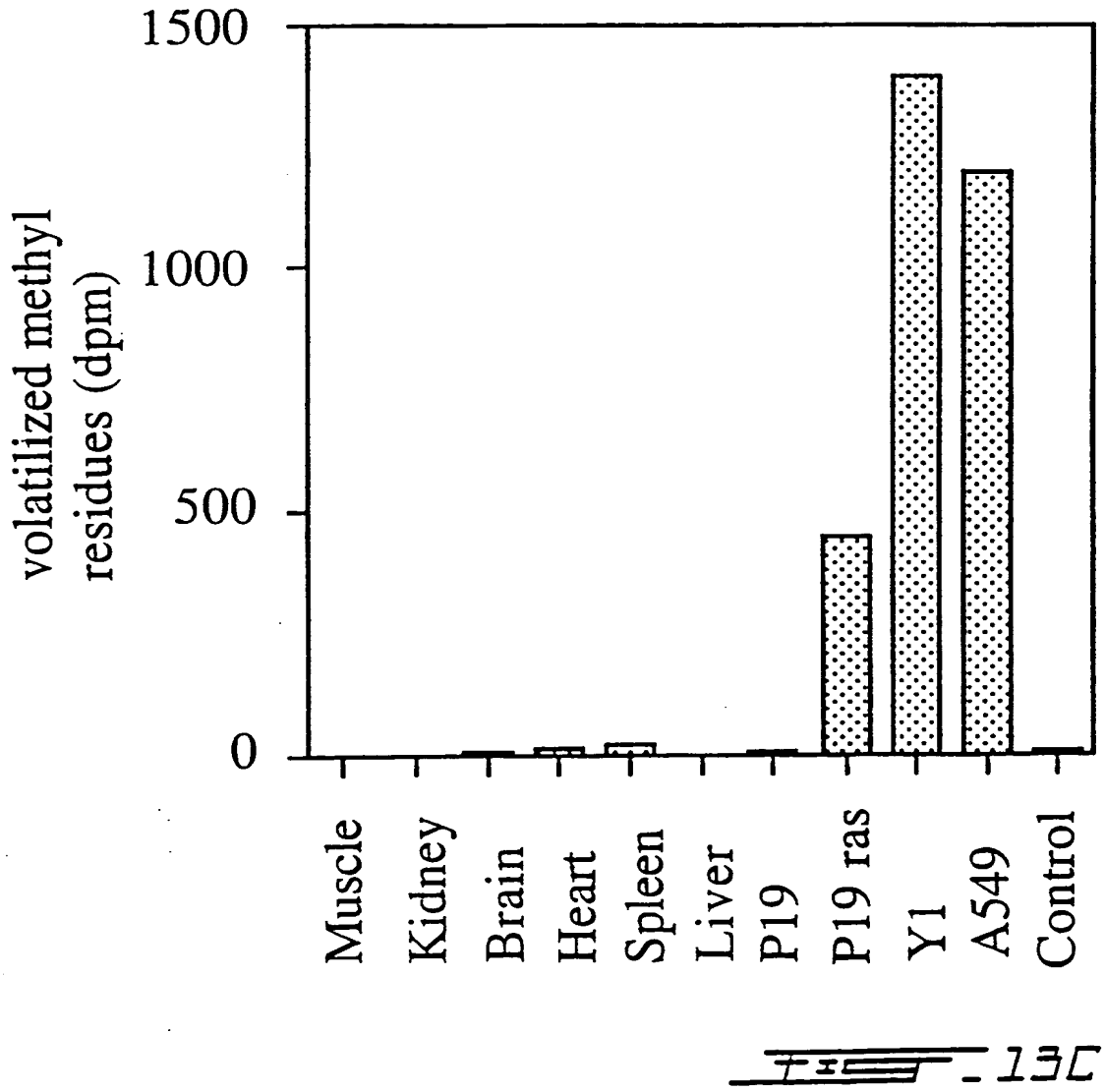

1500
1000
500
0
volatilized methyl residues (dpm)
Muscle
Kidney
Brain
Heart
Spleen
Liver
P19
P19 ras
Y1
A549
Control

FIG. 13C

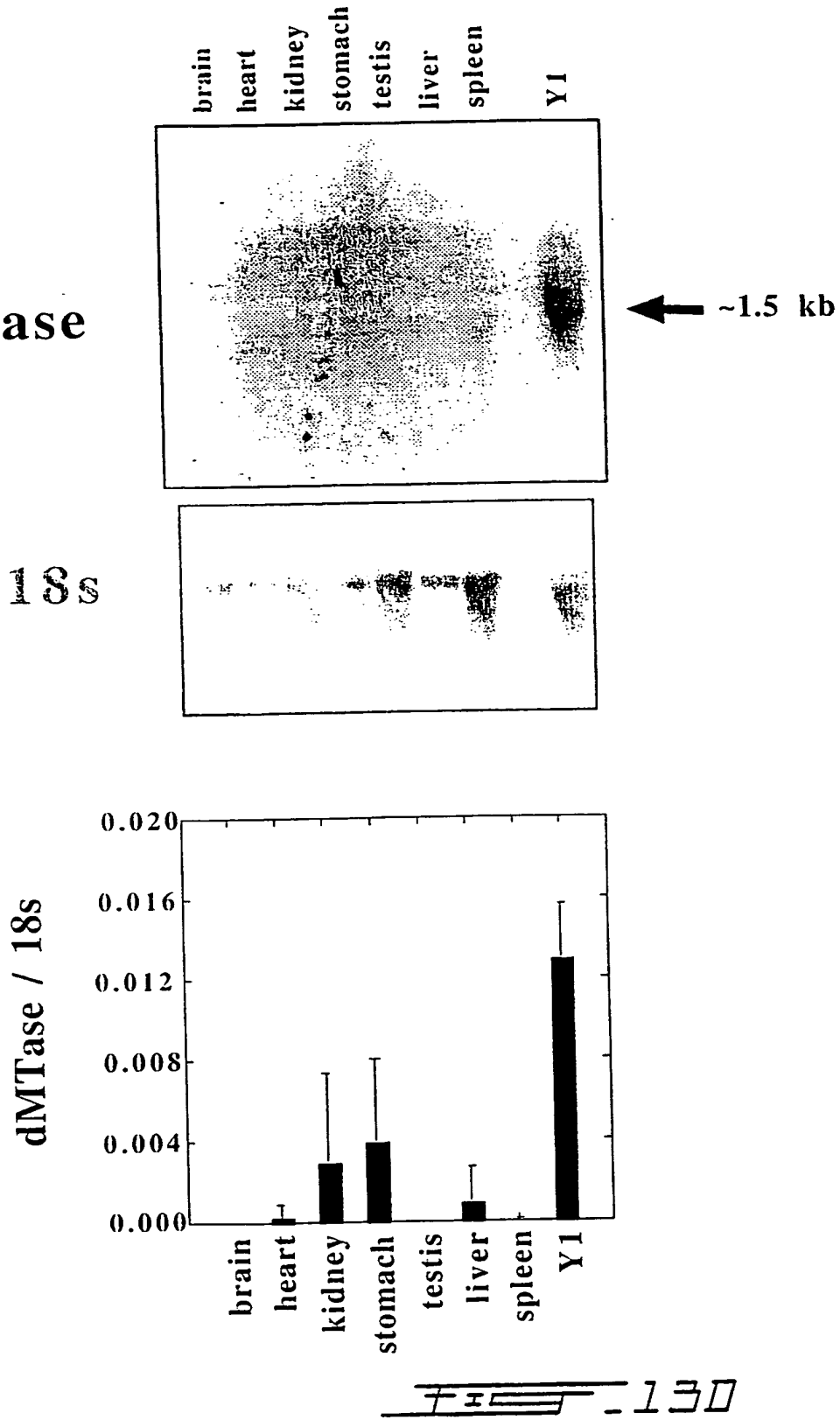
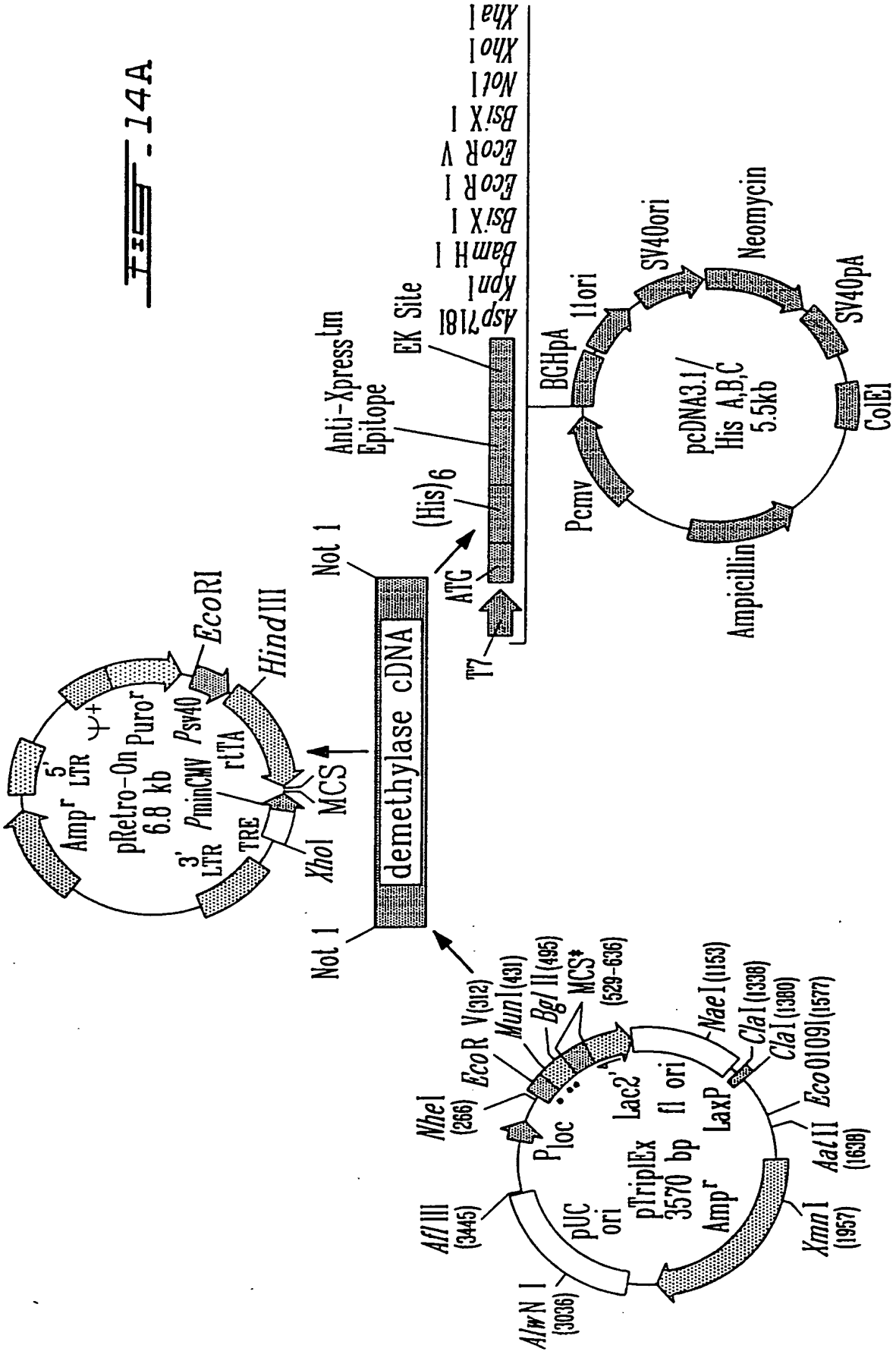

brain
heart
kidney
stomach
testis
liver
spleen
Y1
dMTase
~1.5 kb
18s
dMTase / 18s
0.020
0.016
0.012
0.008
0.004
0.000
brain
heart
kidney
stomach
testis
liver
spleen
Y1

FIG. 13D

FIG - 14A


pRetro-On 6.8 kb
5' LTR
Ampr
ψ+
Puror
Psv40
PminCMV
3' LTR
rtTA
TRE
EcoRI
HindIII
XhoI MCS
Not 1
demethylase cDNA
Not 1
ATG
(His)6
Anti-Xpress tm Epitope
EK Site
Asp718I
KpnI
BamH I
BsiX I
EcoR I
EcoR V
BsiX I
NotI
XhoI
XhaI
T7
BGHpA
11ori
SV40ori
Neomycin
SV40pA
ColE1
Pcmv
pcDNA3.1/ His A,B,C 5.5kb
Ampicillin
pTriplEx 3570 bp
Ampr
pUC ori
Ploc
Lac2'
f1 ori
LaxP
MCS*
(529-636)
Bgl II(495)
MunI(431)
EcoR V(312)
NheI (266)
AflIII (3445)
AlwN I (3036)
NaeI(1153)
ClaI(1338)
ClaI(1380)
Eco0109I(1577)
AatII (1638)
XmnI (1957)

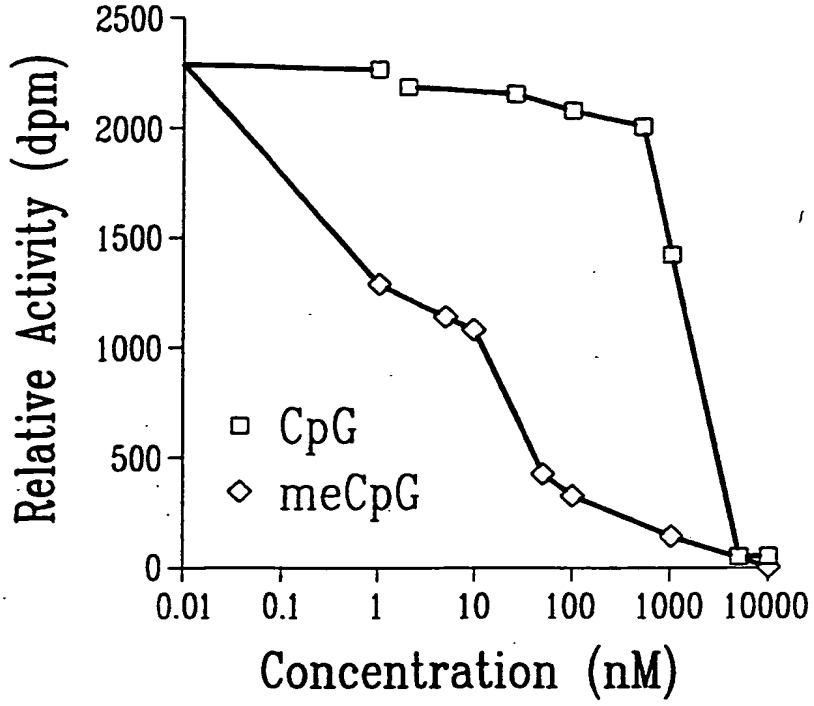


Fig. 14B

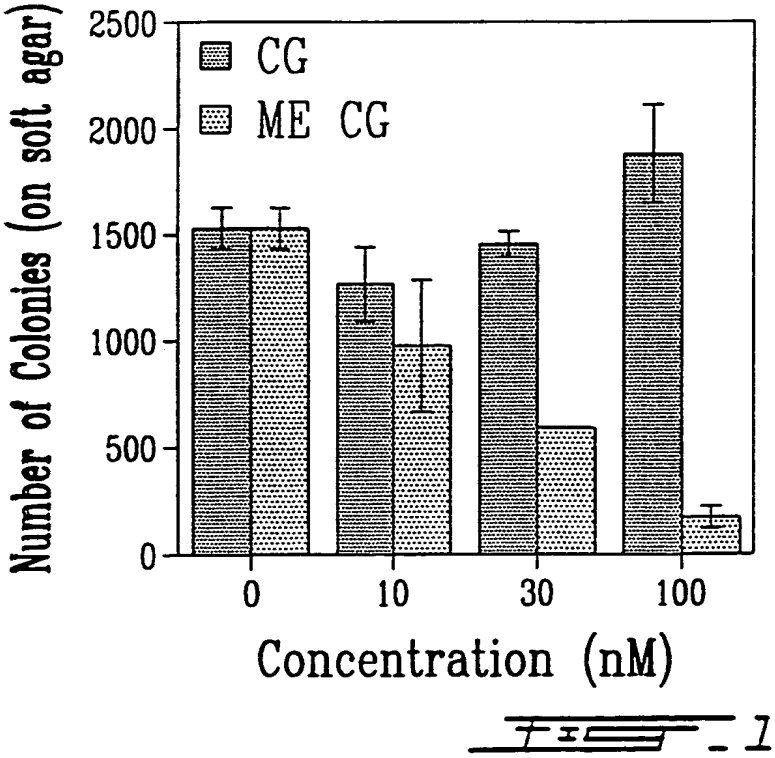
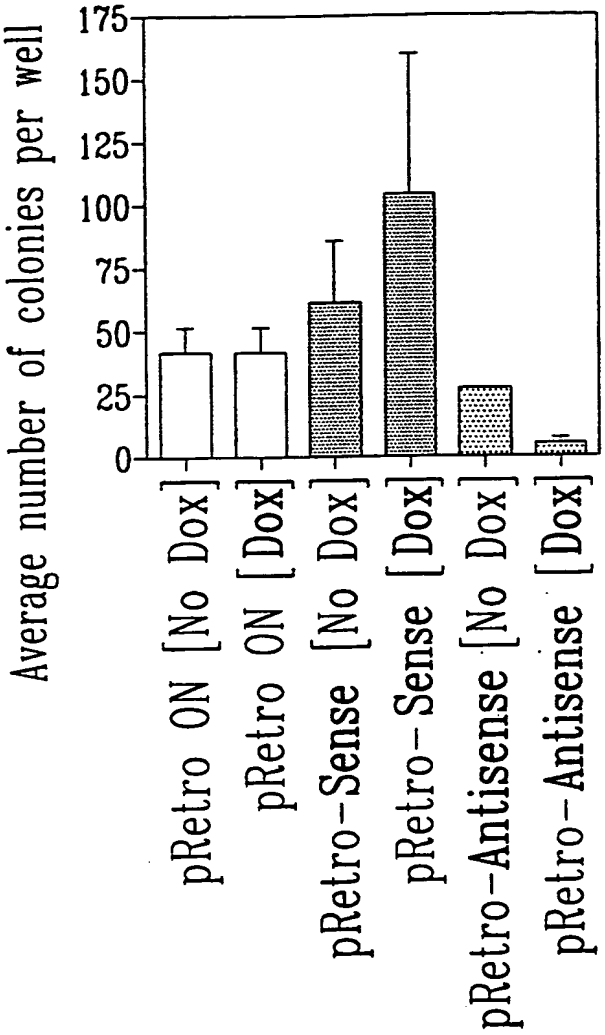


Fig. 14C


Average number of colonies per well
175
150
125
100
75
50
25
0
pRetro ON [No Dox]
pRetro ON [Dox]
pRetro-Sense [No Dox]
pRetro-Sense [Dox]
pRetro-Antisense [No Dox]
pRetro-Antisense [Dox]

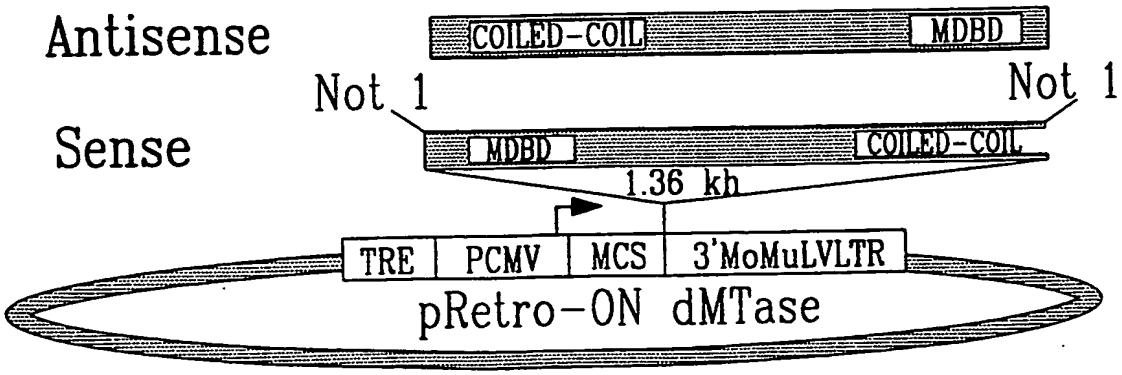

Antisense
COILED-COIL
MDBD
Not 1
Not 1
Sense
MDBD
COILED-COIL
1.36 kh
TRE
PCMV
MCS
3'MoMuLVLTR
pRetro-ON dMTase

Fig. 15

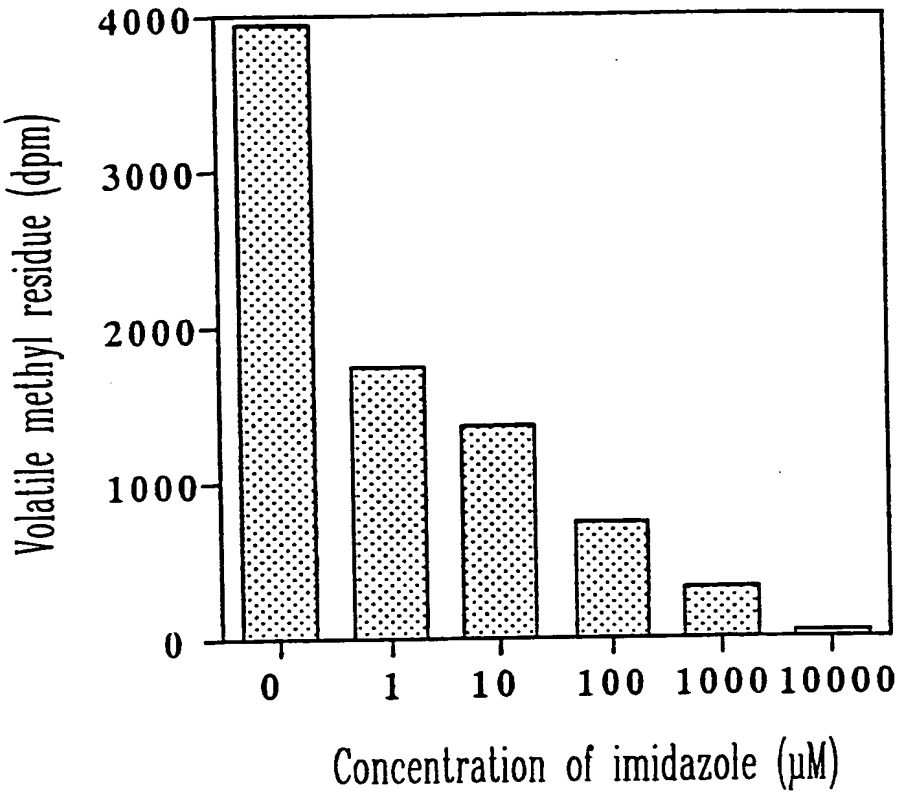

4000
3000
2000
1000
0
Volatile methyl residue (dpm)
0
1
10
100
1000
10000
Concentration of imidazole (μM)

Fig. 16

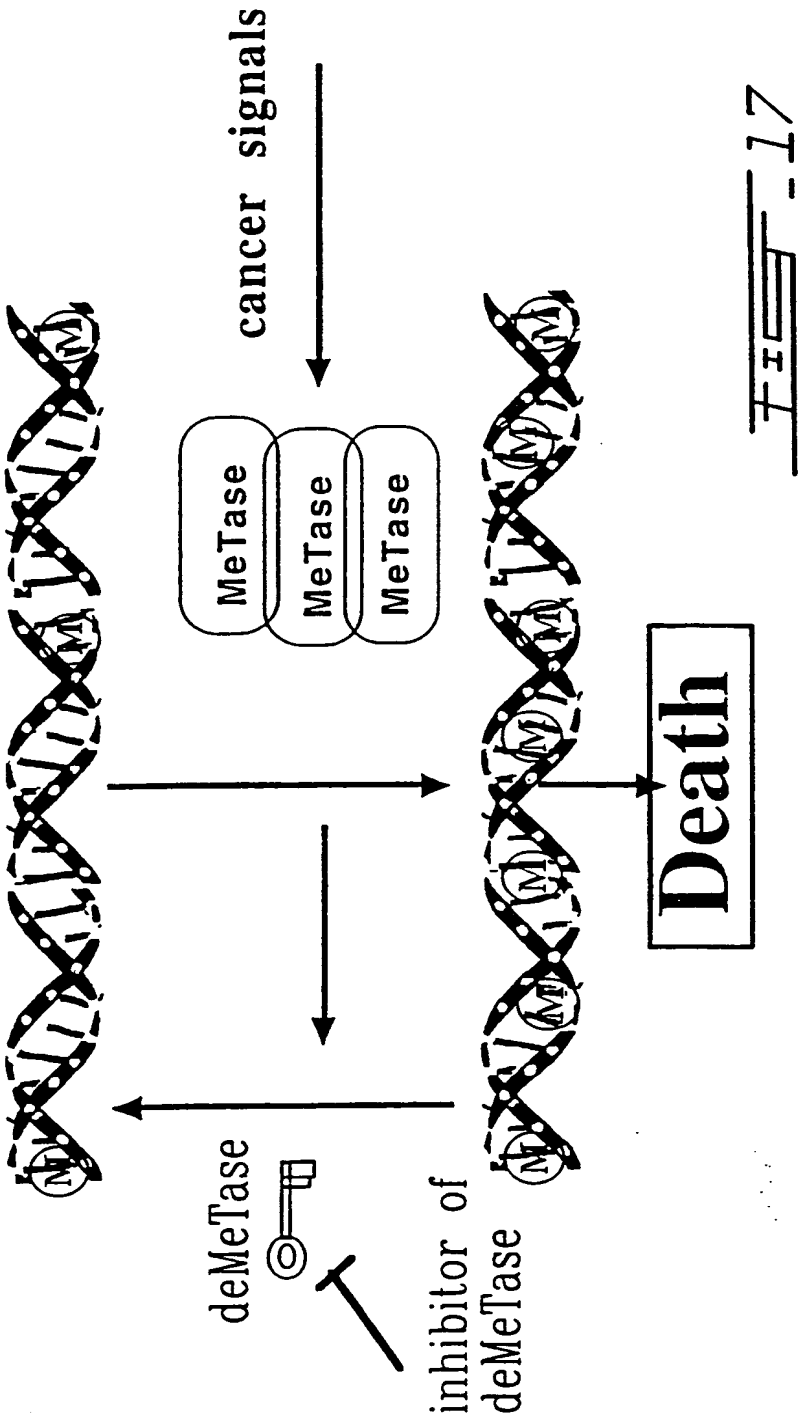


Fig - 17